Remarks

The disclosure was objected to. The patent number has been inserted onto page 1.

Claims 1 to 20 were objected to because "the present Office practice is to insist that each claim must be the object of a sentence starting with 'I (or we),' 'The invention claimed is' (or the equivalent)." Applicant notes that this application was filed electronically and that the Patent Office electronic filing programs (PASAT and EPAVE) do not provide for the insertion of such phrases. Nevertheless, Applicant has inserted "I claim" before the first claim to overcome this objection.

Claims 1 to 6, 8, 9, and 11 to 14 were rejected under 35 U.S.C. §102(b) as anticipated by Coffey et al. ("Coffey"). It is the Examiner's position that the viruses of Coffey would be identical to viruses claimed by Applicant. Coffey's viruses were human reoviruses. They were not modified in any way. They were not genetically engineered, nor were they deliberately evolved by mutating them and selecting from those mutations as in Applicant's process. Coffey's "reovirus requires an activated Ras signaling pathway for the infection of cultured cells." (Abstract) Coffey knew that activating mutations of the proto-oncogene Ras occur in some tumors and injected this unmodified virus into mice that had "tumors established from *ras*-transformed cells.

Not only did Coffey use a virus that had not been modified, but his virus "resulted in regression of tumors in 65 to 80 percent of the mice." In other words, his virus <u>did not attack</u> tumors at all in 20 to 35 percent of the mice. That fact alone establishes that Coffey's unmodified virus is not the same as the viruses claimed by Applicant. The process by which Applicant's viruses are made <u>guarantees</u> that they will attack tumor

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cells. Why? Because tumor cells are put into the loop as target cells and viruses that do not attack those tumor cells are discarded. When the process of modifying the microbes is finished, the only viruses left in the loop are viruses that attack cells from that tumor (and do not attack normal cells). No viruses are removed from the loop as "modified viruses" unless those viruses attack tumor cells (and do not attack normal cells). All of Applicant's claims now include that provision. Thus, Applicant's viruses cannot fail to attack the tumor as Coffey's viruses did in 20 to 35 percent of the mice. Since Coffey's viruses are unmodified and do not attack all the tumors they cannot be identical to the viruses claimed by Applicant.

Claims 1 to 6, 8, 9, and 11 to 19 were rejected under 35 U.S.C. §102(b) as anticipated by Gnant et al. ("Gnant"). Unlike Coffey, Gnant does use a modified virus, a vaccinia virus. The virus was genetically engineered, as described on pages 3396 and 3397. Genetic engineering involves the insertion of DNA (or RNA) known to code for particular desired genes into the genome of the virus. The viruses claimed by Applicant are not genetically engineered. That is, no known strands of DNA are inserted into the virus. In Applicant's viruses, the mechanism by which the viruses attack the target cells and do not attack the cancer cells is unknown. The virus itself either mutates naturally or because it is deliberately mutated in the loop. These mutations do not involve the insertion of known strands of DNA, only random changes in the nucleotides. Virus particles that, due to a mutation, are better able to attack the target cells (and/or avoid attacking the non-target cells) survive in the loop and reproduce; the remaining virus particles are discarded. Thus, it is extremely unlikely that these random mutations will

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produce exactly the same virus particles that are produced by genetically engineering a virus. Indeed, in the case of Gnant, it is not possible. The reason is that Gnatt got a cure rate of "up to 30%," which means that at least 70% of the tumors were not attacked. Viruses that do not attack tumor target cells are not selected in Applicant's process and are not within the scope of Applicant's claims because all of Applicant's claims now require that the modified microbes must attack the target cells and not attack the non-target cells.

Claims 1 to 6 and 8 to 20 were rejected under 35 U.S.C. §102(a) as anticipated by Heise et al. ("Heise"). Heise, like Gnant, genetically engineers a virus and the hereinabove comments about Gnant apply to Heise as well.
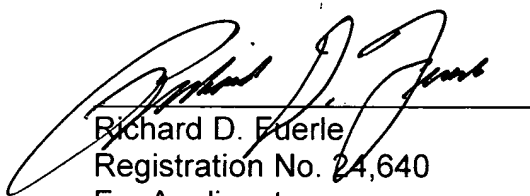
Claims 1 to 20 were rejected under 35 U.S.C. 112, first paragraph. The Examiner argues that some microbes may not be capable of being modified as described by the process of the invention to attack target cells, but not non-target cells. Applicant's invention works by the process of evolution. Evolution can take a simple organism and evolve it into a more complex organism or take a complex organism and evolve it into a simpler organism. All of the microbes are, by definition, "alive" in the sense that they can replicate. They are therefore mutatable and the mutations are subject to the selections made in the process of the invention. While it may take much longer to modify microbes that are not already infectious, there is no reason, in principle, why it would not occur. Nevertheless, Applicant has limited all of his claims to "disease-causing" microbes or viruses (see paragraph [0019], line 1, for support), to overcome this rejection. All of Applicant's claims also require that the modified microbes must

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attack target cells and not attack non-target cells so, if the Examiner is correct that some microbes cannot be modified in that way, then those viruses would be outside the scope of Applicant's claims.

Claims 1 to 20 were rejected under 35 U.S.C. 112, second paragraph. The Examiner asserts that the word "modified" is not clearly defined. Applicant's entire specification explains how microbes are modified according to the invention. All of Applicant's claims explicitly specify the steps used to modify a microbe. Applicant does not see how a person who is skilled in the art can not understand what Applicant means by the word "modified."

Applicant believes that all the claims, as amended, should now be allowable. If the Examiner does not agree, he is invited to call Applicant's attorney at (716)-774-0091 to resolve any remaining issues.

Respectfully,

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